profoundly influence the ideals, the methods and character of academic and professional education.

The concluding session of the meeting was an informal conference of deans of graduate schools for discussion of questions of policy and administration for mutual enlightenment and better understanding of their common problem, how best to foster the most advanced work done in our universities. Such a conference as this had been held at previous meetings and had been found to be so necessary that a number of deans of graduate schools were in attendance at their own expense who were not delegates to the association. The questions arising in the administration of graduate schools are so new and important that it is extremely desirable to put the united wisdom and experience of all at the disposal of each, as can be accomplished in no way so well as the free and informal interchange of a round table conference. The meeting as a whole was most useful in bringing together and helping to fuse into a consensus of opinion and action the men controlling the leading universities of the country.

The annual report to be published later will contain the papers and discussions in full, excepting the conference of deans.

H. T. EDDY

SPECIAL ARTICLES

THE RÔLE OF DIFFERENT PROTEINS IN NUTRITION AND GROWTH

INTEREST in the study of the problems of nutrition has largely been coincident with the development of the chemical aspects of physiology, in distinction from the physical and mechanical phenomena which earlier attracted the attention of investigators. The subject of nutrition has, in large measure, been considered in the past from what might be designated as a statistical standpoint. The balance of income and outgo of energy and matter, nutritive needs and dietary standards, and the effect of external factors on these, are illustrations of the type of questions which has called for discussion. With the progress in the study of physiological chemistry have come important additions to our knowledge of the make-up of the foodstuffs and of the real significance of the processes which take place in the alimentary tract. The conception of digestion as a simple act of solution has evolved into that of an intricate and carefully regulated chemical transformation. The intermediary changes which characterize the metabolism of food materials after absorption and incident to the real nutritive reactions of the body within its tissue cells have at length become the subject of experimental inquiry.

With this development has come about an appreciation of the *specific* rôle of foodstuffs. Various incidents have favored this trend of physiology. The study of enzymes and their striking specificity has served to emphasize the necessity of digestion before the nutrients can satisfy their purposes. Observations on the unique responses of various parts of the alimentary tract to different kinds of chemical compounds have brought to light the remarkable interrelations of the secretory and motor functions of the digestive tract and their dependence on special (chemical) stimulants. But more important than all this, perhaps, have been the disclosures of the past decade in respect to the chemical structure of the so-called proximate principles, and the proteins in particular. The development of this field of study has been little short of epoch making, so that it seems timely to begin to apply some of the newer knowledge to the investigation of problems in nutrition.

The idea that proteins of different origin may possess an unlike physiological value is not entirely new. Gelatin, for example, has long been pointed out as an illustration of an inadequate protein. It has been impossible experimentally to sustain life with a diet in which gelatin formed the sole source of nitrogenous intake. To-day one can cite other illustrations of proteins, *e. g.*, zein, gliadin, hordein, casein, which lack some of the characteristic amino-acid complexes readily obtainable from other albuminous materials which are vaguely regarded as "complete." In still other cases, *e. g.*, edestin and glutenin,

the relative proportions of these constituent complexes are so markedly different from the average as to raise the question of comparative nutrient values. Overabundance of glutaminic acid groups must necessarily be attended by relative deficiency in other so-called "building stones" of the protein fundament. If, then, a minimum of some of these is an indispensable requirement of tissue maintenance or growth or repair, problems of relative values at once suggest themselves.[1] To this may be added the question of protein synthesis in animals which has been so vigorously debated in recent years. Here we touch upon problems quite independent of the energy needs of the organism, yet equally important. No sooner has the idea of the isodynamic replacement of nutrients found acceptance, than the practical limitations of this law are subjected to critical examination.

The foremost reason why so little is known in the directions noted lies in the fact that the individual foodstuffs have, with very few exceptions, rarely been examined heretofore in respect to their actual nutrient rôle. Meat and cereals have, it is true, been crudely analyzed in terms of protein ($N \times 6.25$), fat, carbohydrate and ash, and fed as assumed mixtures of the composition indicated. Physiologists are, however, just beginning to recognize the extreme chemical complexity of such animal and plant tissues. How much of the nutritive failures or successes shall be ascribed to either presence or paucity of some incidental component, as lime or iron, as lipoid or nitrogenous "extractive" of specific physiological import, such as is attributed to the "hormones"?

It is, indeed, only in very recent years that the perfection of biochemical technique has permitted the preparation of isolated proteins in what may be called comparative purity. We believe, from the experience which one of us has gained during many years of experiment in this field, that the vegetable proteins to-day are in general easier of access for chemical investigation and isolation than the related compounds of animal origin. And it is this fact which encouraged us to undertake what Carl Voit long ago proclaimed as the ideal method, viz., the feeding of isolated foodstuffs under controllable conditions. The laborious and costly investigations which are under way have been made possible by the cooperation of the Carnegie Institution of Washington. A detailed report of the first two years' work and the literature pertaining thereto is available in Publication 156, Parts I. and II., of the Carnegie Institution.[2] The following pages are intended to call attention very briefly to some aspects of these studies.

We have undertaken to investigate certain features of nutrition by feeding isolated food substances to albino rats. The selection of this animal has been determined by several in part obvious considerations. The white rat is easily reared and cared for. Its small size reduces the food requirement to a magnitude which falls within the range of experimental possibility where the preparation of special dietaries by laborious processes is a fundamental prerequisite. Furthermore, the longevity of this animal is, according to Donaldson, about three years; so that the first year of life corresponds to a long span in terms of human years. Not insignificant is the additional fact that the white rat has in recent years been made the subject of exceptionally extensive measurements in respect to growth and various features of development at the Wistar Institute in Philadelphia. In this way physical standards, so to speak, have been established for this animal.

At the outset numerous problems of experimentation have arisen quite apart from the main question itself. Can rats be kept in health indefinitely under cage conditions which permit the control of the food intake and collection of the excreta? For the description of the cages and experimental technique we must

[1] These and related questions are discussed in detail by Mendel, "Ergebnisse der Physiologie," 1912, XI.

[2] "Feeding Experiments with Isolated Food-substances," by Thomas B. Osborne and Lafayette B. Mendel, with the cooperation of Edna L. Ferry, Carnegie Institution of Washington, Publication 156, Parts I. and II., 1911.

refer to our detailed publication (Part I.). How successful this has been is best answered by the statement that rats have been maintained for many months at all ages with apparent success. Far more important than the ability to withstand confinement in a restricted space has been the demonstration of the possibility of maintaining rats on an "artificial" food paste of unaltered uniform composition during a large span of their life. Herein we have apparently been far more successful than any of our predecessors; for the supposed *monotony* of diet has been the stumbling block leading to failure in the records of various investigators.[3] Their animals have failed to eat and have declined as an obvious result of insufficient food intake. We are inclined to lend emphasis to the result of the excellent hygienic environment and care of our animals. And whereas nutritive decline has commonly been attributed to the anorexia consequent upon the monotony of diet, we are more than ever inclined to shift the explanation in many such cases to malnutrition as a primary cause. From this point of view improper diet and malnutrition may be the occasion rather than the outcome of the failure to eat—a distinction perhaps not sufficiently recognized heretofore.

As the criterion of the nutritive status of the rats their body weight has been adopted, and this has proved to be an advantageous index. It soon became apparent that one must distinguish sharply between maintenance and growth in any such study of nutrition. The white rat shows a very characteristic curve of growth (plotted from the body weight) which becomes practically stationary within 300 days. According to Donaldson the body weight changes from 5 grams at birth to 270 grams in the case of the male, or 225 grams in the female at the age of 300 days. To judge of the effect of a dietary régime by noting the subsequent duration of life, as is still frequently done by investigators, is misleading; for the incidence of death may depend on the previous nutritive condition—the store of fat and glycogen—where food is insufficient. An error less readily appreciated consists in describing the nutritive status as necessarily satisfactory because an animal maintains an undiminished body weight over long periods under the conditions imposed. A man who maintains his weight may be in excellent nutritive condition; but a child which does likewise is *failing to grow*. Childhood demands of a perfect ration the possibility of normal *growth,* not simply *maintenance.* This can not be emphasized too strongly. Furthermore, growth in the sense of an increase in the size of some structural part of the body or some organ may proceed independently of the correlated development of the body as a whole. Even with the existence of unquestionable malnutrition, skeletal growth may manifest itself in a conspicuous degree; so that the length or height of an individual may markedly increase while the total body weight remains stationary or even declines. One part of an organism may thrive at the expense of other tissues. The complexity of these relationships of absolute and relative (or proportionate) growth have likewise commanded attention in our experiments.

A study of physiological literature will make it evident that no convincing reply has been given to the question: can life be maintained and is growth possible with a *single* protein in the dietary. "Protein" has been used in this connection in a generic sense; and one of the (chemically) simplest foods, milk, contains at least two proteins of marked individuality. Casein and lactalbumin are chemically unlike. How widely two extensively used food proteins may differ in their chemical make-up is indicated below.

The individuality of proteins of different biological origin is further indicated by their specific immunity reactions. The published feeding experiments in which a single purified protein has been administered to animals are all limited in their duration to periods of days or weeks which are too brief to furnish convincing data. Indeed, one will scan the literature in vain for properly controlled experi-

[3] These earlier studies are reviewed in Publication 156, Part I., Carnegie Institution of Washington, 1911.

Amino-acids	Casein[4] Per Cent.	Zein[5] Per Cent.
Glycocoll	0.00	0.00
Alanine	1.50[4]	9.79
Valine	7.20[4]	1.88
Leucine	9.35[6]	19.55
Proline	6.70[7]	9.04
Aspartic acid	1.39[4]	1.71
Glutaminic acid	15.55[4]	26.17
Phenylalanine	3.20[8]	6.55
Tyrosine	4.50[9]	3.55
Serine	0.50[10]	1.02
Oxyproline	0.23[10]	——
Histidine	2.50[11]	0.82
Arginine	3.81[11]	1.55
Lysine	5.95[11]	0.00
Tryptophane	1.50[8]	0.00
Diaminotrioxydodecanic acid	0.75[12]	——
Ammonia	1.61[13]	3.64
Sulphur	0.76[14]	0.60
Phosphorus	0.85[14]	0.00

ments in which isolated and purified proteins have been fed successfully.[15]

Without citing here the numerous failures and the successive changes instituted in our earlier trials, we may briefly call attention to some of the purely "nutritive" factors which have had to be taken into consideration. The energy requirement must obviously be satisfied in an *available* form. A minimum protein requirement must likewise be provided in any event. Experiments which are to continue over more than very few days must include a *suitable* quota of inorganic salts—so-called mineral nutrients. This is in itself a problem of fundamental importance, the study of which has barely been begun in any synthetic way. One may, it is true, imitate the "ash" of milk or blood; but the elements occur here in combinations quite different from those prevailing in the tissue fluids themselves or in the native foods. The balance of acid and basic groups, the changing need for individual elements like phosphorus, calcium, chlorine and iron, furnish a series of complex variables which are probably as indispensable to certain aspects of nutrition as they are unappreciated. If to all this is added the uncertain significance of the as yet largely unidentified compounds such as cholesterol and phosphatides which occur in all natural food mixtures, the experimental difficulties begin to appear in their true light.

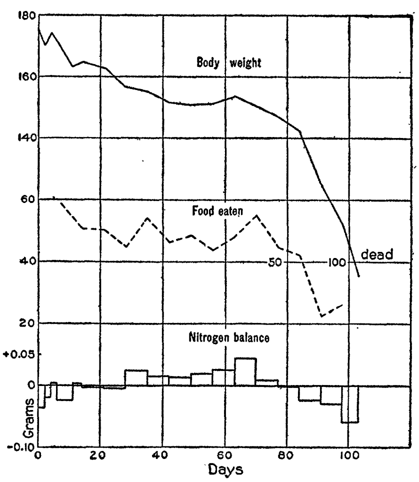


FIG. 1. (Taken from Carnegie Publication No. 156, page 26.) Showing the continued decline of a rat on a dogbiscuit-lard diet for 103 days.

At the outset it is only fair to remark that a successful feeding experiment with isolated food mixtures is of greater import than a

[4] Osborne and Guest, *Journal of Biological Chemistry*, 1911, IX., p. 333.

[5] Osborne and Liddle, *American Journal of Physiology*, 1910, XXVI., p. 304.

[6] Levene and Van Slyke, *Journal of Biological Chemistry*, 1909, VI., p. 419.

[7] Van Slyke, *Berichte der deutschen chemischen Gesellschaft*, 1910, XLIV., p. 3170.

[8] Abderhalden, *Zeitschrift für physiologische Chemie*, 1905, XLIV., p. 23.

[9] Reach, *Virchow's Archiv*, 1899, CLVIII., p. 288.

[10] Fischer, *Zeitschrift für physiologische Chemie*, 1903, XXXIX., p. 155.

[11] Osborne, Leavenworth and Brautlecht, *American Journal of Physiology*, 1908, XXIII., p. 180.

[12] Fischer and Abderhalden, *Zeitschrift für physiologische Chemie*, 1904, XLII., p. 540.

[13] Osborne and Harris, *Journal American Chemical Society*, 1903, XXV., p. 323.

[14] Hammarsten, *Zeitschrift für physiologische Chemie*, 1883, VII., p. 227.

[15] Cf. Osborne and Mendel, Publication 156, Part I., Carnegie Institution of Washington, 1911, for the literature on these topics.

failure may be; for ill health may be occasioned by incidents quite apart from those already outlined. Accident and acquired disease, unrecognized or uncontrollable, enter into the life of every individual and serve to upset an otherwise normal nutritive equilibrium.

Turning to the present experiments, our earlier attempts were largely based on those of our predecessors. Comparative trials with food mixtures precisely alike except for both content and character of the inorganic ingredients soon showed the great importance of this feature. A fairly suitable salt mixture was thus empirically selected. The table below may serve to illustrate the character of the earlier food mixtures which experience showed to be most suitable.

In such a mixture the protein can be varied without serious change in the fuel value. With one protein, viz., zein from maize, nutritive decline was apparent from the outset. The failure, as actual investigation showed, can not be attributed solely to poor utilization. With all the other proteins, such as casein, legumin, edestin, glutenin or gliadin, in the mixtures indicated, grown rats have been

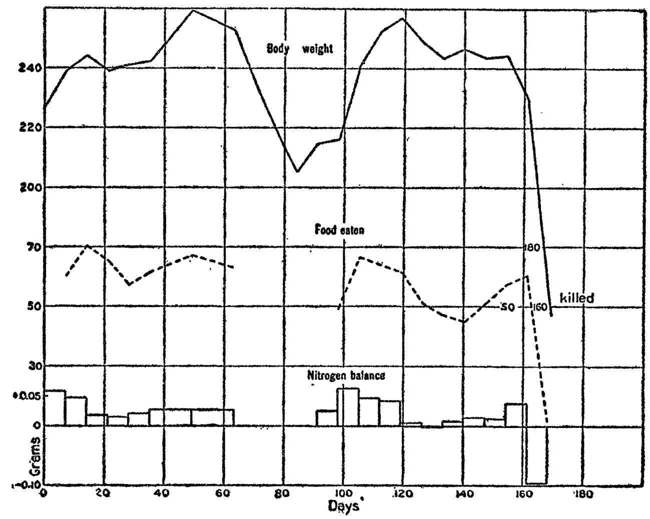


FIG. 2. (Taken from Carnegie Publication No. 156, page 42.) This rat was fed for 169 days on a diet containing pure casein as the only protein.

	Per Cent.
Isolated protein	18
Cane sugar	15
Starch	29.5
Lard	30
Agar-agar[16]	5
Salt mixture	2.5
	100.0

[16] This indigestible carbohydrate was added to furnish "roughage" in the diet. Cf. Mendel, *Zentralblatt für Stoffwechsel*, 1908, No. 17; Swartz, "Nutrition Investigations on the Carbohydrates of Lichens, Algæ, and Related Substances," *Transactions Connecticut Academy of Arts and Sciences*, 1911, XVI., pp. 247–382.

maintained in body weight for much longer periods than we have found recorded by previous investigators.

From many protocols we present three in graphic form; the first to illustrate a failure from the outset, the second and third as examples of a relatively successful attempt over a period of 169 days and 259 days, respectively.

In every case—and we might cite very many such experiments under varied conditions—a decline ultimately ensued leading to death unless a dietary change was instituted.

It early seemed unlikely that the protein was responsible for failures of this character; for this foodstuff forms so large an essential

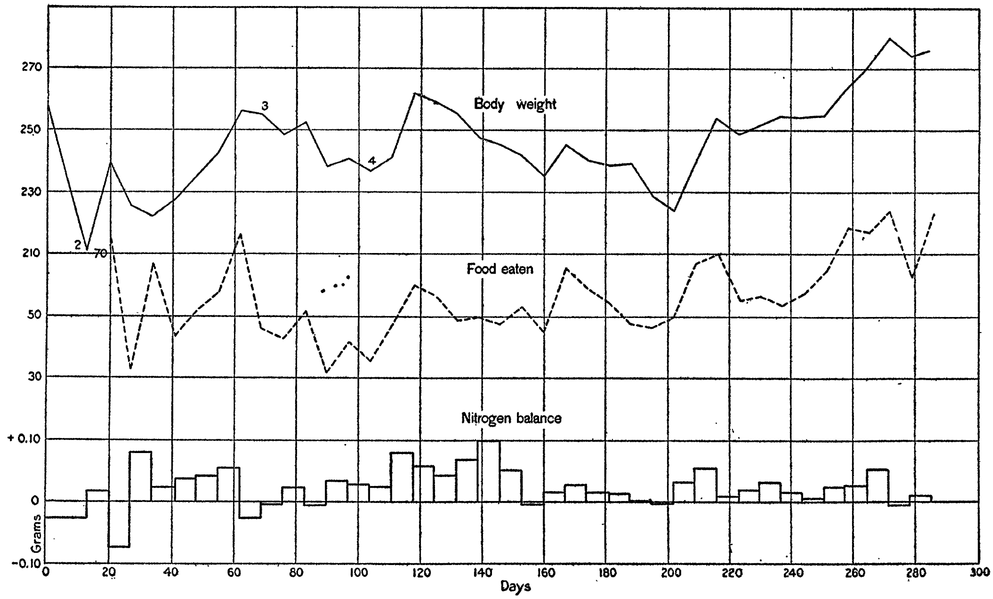


FIG. 3. (Taken from Carnegie Publication No. 156, page 49.) This rat was fed 69 days on a diet containing casein and glutenin as the sole proteins, followed by a period of 259 days in which glutenin formed the sole protein of the diet. Only a portion of the duration of this experiment is reproduced in the figure.

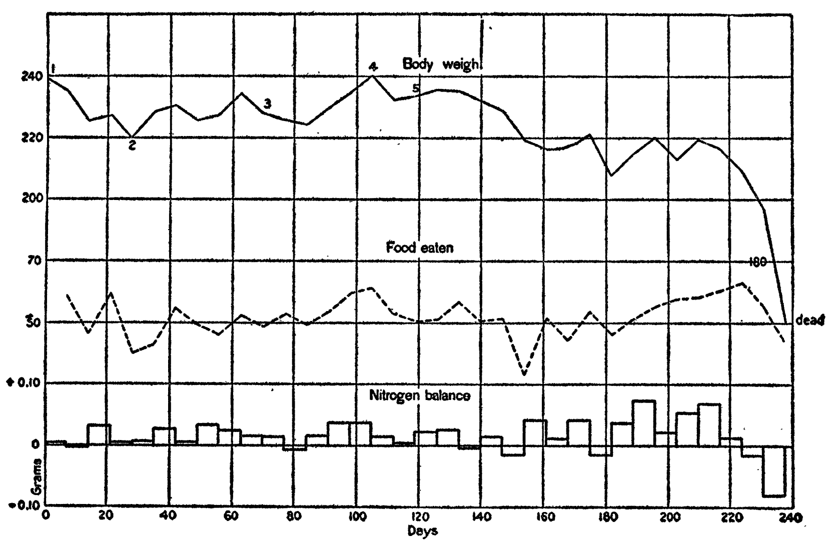


FIG. 4. (Taken from Carnegie Publication No. 156, page 45.) This rat was fed 210 days on a diet containing casein and excelsin as the only proteins.

component in the mixture that a defect ought soon to manifest itself—as indeed it did with zein. Nor did the animals fare better when more than one protein was present. Here, too, the ultimate decline in the grown rats inevitably showed up, as will be seen in the illustrative charts below.

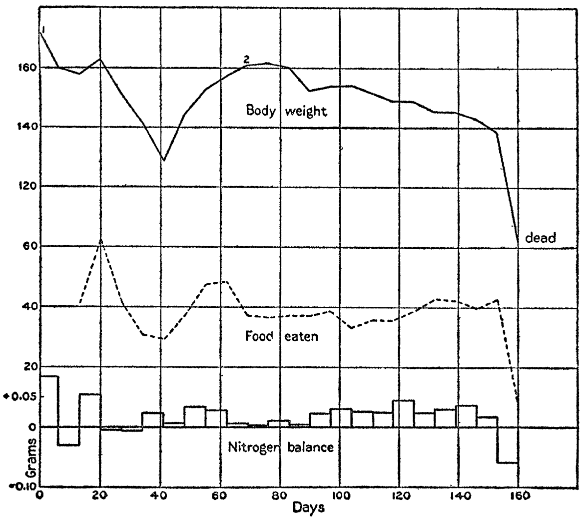


FIG. 5. (Taken from Carnegie Publication No. 156, page 46.) This rat was fed 160 days on a diet containing casein and pea legumin as the only proteins.

Remarkable in this connection were the observations made on small white rats during the period of active growth. Lacking food, at this stage, the animals speedily die, since the reserve stores are small or wanting. With an appropriate mixed diet growth is vigorous, and the rate of gain is strikingly similar in healthy animals of related origin. When young rats are fed on diets containing a single protein in the mixtures described above they *fail to grow,* although they can be maintained at uniform body weight and size for long periods. Here then is an evident distinction between *maintenance* and *growth* in respect to the function of the ration. An illustration of the stunting of animals in this manner is graphically afforded by the appended curves in which a dwarfed animal is compared with a suitably fed one from the same litter.

What is the factor or what are the causes connected with the ultimate failure of the older rats to thrive on the dietaries outlined, or of young rats to grow? Evidence which

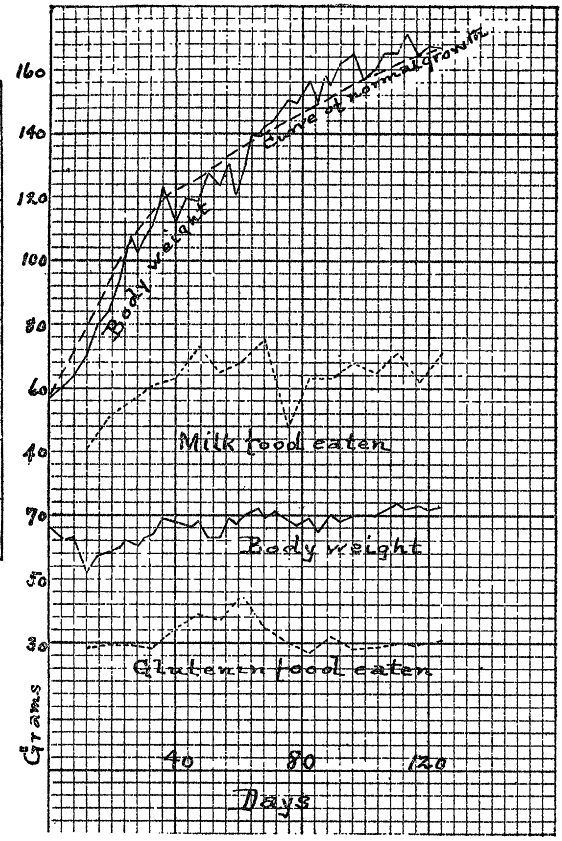


FIG. 6. Showing the body weight and food intake of a small rat grown normally on a diet of dried milk and lard in the upper curves. The lower curves are charted from a rat of the same litter maintained without growth on a diet containing glutenin as the sole protein in a mixture unsuitable for growth.

need not be reviewed here pointed to something other than the character of the protein, fat or carbohydrate. Animals will thrive and grow on a "mixed" diet of corn, vegetables, etc.; but we have, furthermore, noted that their nutritive needs can be met with an "artificial" food mixture in which dried milk and

fat form the sole ingredients.[17] That the stunted or malnourished rats in these earlier experiments have not lost their *capacity to grow* or, in the case of the adults, have not become permanently disorganized from a nutritive standpoint can be readily demonstrated; for they will resume growth or become realimented, as the case may be, as soon as mixed food is furnished. The milk mixtures are as efficient as mixed food in promoting growth and restoring nutritive equilibrium.

Rats have been carried through two generations on a food mixture of the following composition:

	Per Cent
Milk powder	60.0
Starch	15.7
Salt mixture	1.0
Lard	23.3
	100.0

Obviously the milk contains the nutrient elements essential to success which had previously not been satisfactorily imitated in the artificial food mixtures. It occurred to us to attempt to locate these as yet unknown components by removal of the proteins from milk and concentration of the protein-free (and fat-free) residues. The product thus obtained (and which may conveniently be termed "protein-free milk"[18]) has fulfilled our expectation and enabled us at length to study the relative value of added proteins in the dietary. The protein-free milk contains the milk sugar in addition to inorganic salts and other as yet unknown components of the milk. Whether

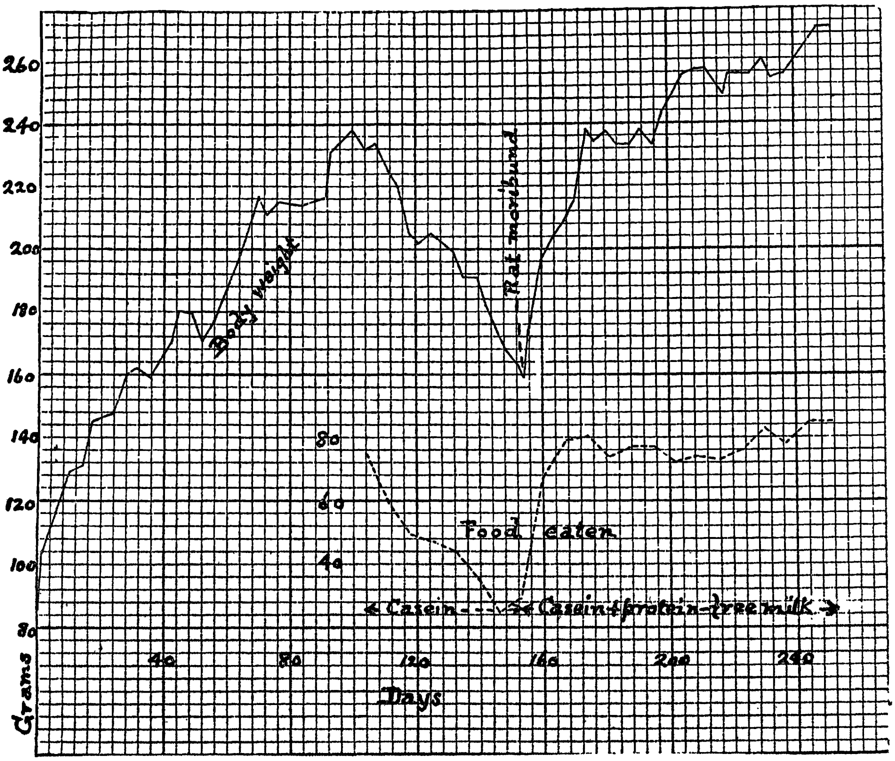


FIG. 7. Showing the realimentation of a rat practically moribund, by the addition of protein-free milk to the diet containing a single protein (casein).

[17] The dried milk used is the commercial "Trumilk," furnished by the Merrell-Soule Co., of Syracuse, N. Y.

[18] A detailed description of the preparation and composition of protein-free milk is given in the detailed papers, Part II.

it is the peculiar combinations of the latter, or some ideal "balancing" of the inorganic ions therein, or the presence of traces of essential organic compounds, or all of these, which guarantee the successful outcome, remains to be ascertained.

What has been accomplished thus far with the new possibilities of investigation at hand may be mentioned in brief. Rats which have developed marked symptoms of decline on mixtures of isolated food substances containing a single protein have been revived in a way little short of marvelous by the substitution of the protein-free milk in place of part of the previous (non-protein) food. Instances have occurred where successful realimentation has thus followed in animals practically moribund. The chart below furnishes a graphic illustration.

Even more interesting is the rôle of this protein-free milk in facilitating growth. By the use of protein-free milk to furnish the "accessory" portions of the diet the relative deportment of different proteins in growth has been investigated. Thus adequate growth has been noted where the sole protein was either the casein of milk, the lactalbumin of milk, crystallized egg albumin, crystallized edestin from hempseed, the glutenin of wheat, or glycinin from the soy bean. But *not all proteins suffice to promote growth* under otherwise favorable conditions. The gliadin of wheat (notably lacking in glycocoll and lysine) and the hordein of barley (closely resembling gliadin in its chemical constitution) suffice for maintenance without growth. Zein, the tryptophane-, lysine- and glycocoll-free protein of maize, is alone insufficient for the maintenance requirement. How well growth can proceed under these somewhat artificial condi-

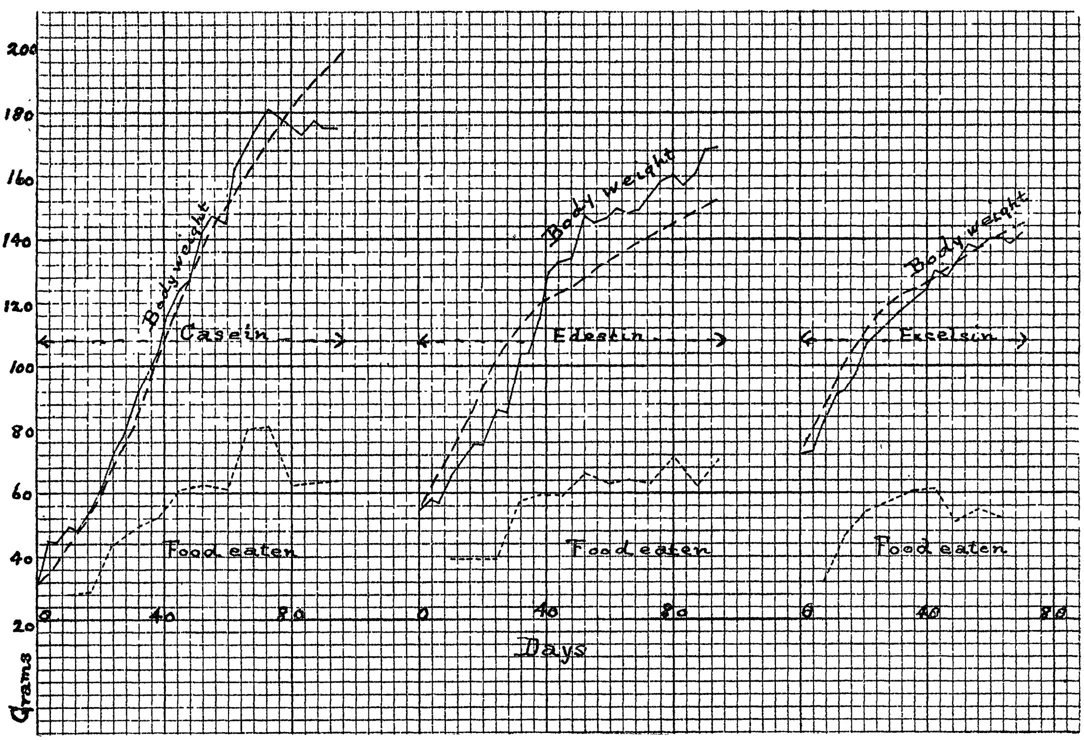
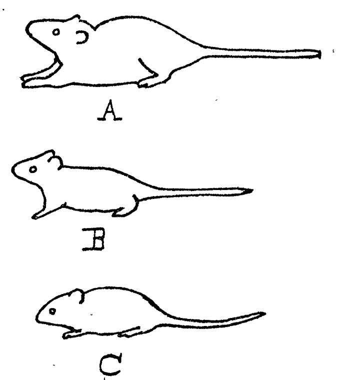


FIG. 8. Showing the growth curves of young rats fed on a diet containing a single protein together with protein-free milk. The upper broken lines in each figure indicate the normal rate of growth on mixed food.

tions of diet is shown in a few charts in which the curve of growth on mixed food is simultaneously plotted.

How entirely different the results are when an "inadequate" protein is alone furnished, despite an abundant ingestion of food, is strikingly shown by the drawings. The animals *A* and *B* were of one age and differed simply in having been sustained on different proteins.



This drawing shows the influence of different proteins on growth. *A* and *B* are rats of the same brood which were fed from the time of weaning on foods of the same composition except that the diet given to *A* contained pure *casein* while that given to *B* contained pure *gliadin* as its only protein. The appearance of *B* at the age of 140 days closely resembles that of *C*, a normally nourished rat, which at the age of 36 days had the same weight as *B*. (Sketch from photographs in Publication 156, Part II., Carnegie Institution of Washington, 1911.)

It will be noted that the older but stunted animals do not vary materially in size from properly nourished younger animals which have attained the same body weight. Herein they differ essentially from young animals which, maintained at constant body weight by underfeeding, continue to grow in size. Such conditions have been described in cattle,[19] dogs[20] and children;[21] and they lead to disproportioned forms. Our (malnourished rather than undernourished) rats have merely maintained themselves, if we except the possibility of a continued development of the nervous system of which we have furnished some evidence elsewhere.[22]

Aside from the nutritive inequalities of different proteins, as well as the apparent comparable suitability of chemically and biologically unlike proteins—all of which remains to be subjected to more refined experimental investigation—it is worth while to point out numerous other incidental findings. Animals which have grown from small size, *e. g.*, 40 grams, to adult form, *e. g.*, 160 grams, and have thus quadrupled their weight on a diet furnishing its nitrogen in the form of a simple protein like edestin, have by some process perfected the synthesis of purines and nucleoproteins, perchance of phosphoproteins and nitrogenous phosphatides, and of ferruginous proteins (like hemoglobin) from iron-free protein precursors and "inorganic iron."

With what powers of synthesis in such directions is the body provided by nature? What modifications, if any, can be introduced into the organism in respect to structure, function or inheritance by the possibility of a successfully regulated control of the character of the most important foodstuff, the protein? Such physiological and broader biological questions appear to lend themselves to experimental study by the methods which we have initiated. There are, further, pathological aspects involving abnormal growth, dwarfism, recuperation and senescence which similarly suggest themselves. The program for the future is limited only by the success and efficiency of the methods adopted.

To the biological chemist, no feature of these problems appeals more strongly, perhaps, than the question of how an organism can build such diverse nitrogenous tissues from a

[19] Waters, *Proceedings Society for the Promotion of Agricultural Science*, 1908, XXIX., p. 3; also *Ibid.*, XXX., p. 71.

[20] Aron, *Biochemische Zeitschrift*, 1910, XXX., p. 207; *Philippine Journal of Science*, Sec. B., 1911, VI., p. 1.

[21] Fleischner, *Archives of Pediatrics*, October, 1906.

[22] Osborne and Mendel, Carnegie Institution of Washington, Publication 156, Part II.

single dietary protein. It is true that the newer conceptions of the extensive rôle of hydrolysis in digestion prior to absorption have extended the inquiry a step further, so that we may ask what is the minimum of this or that amino-acid or simple polypeptide required. But we have seen rats grow for months with casein—thoroughly purified and glycocoll-free—as the sole source of these amino-acids. During this time, one animal even brought forth two broods of young and secreted milk in sufficient quantity to bring her young to the age when they were able to care for themselves. Another pair of rats maintained 178 days on gliadin as the sole protein of the diet produced healthy young and successfully reared them. It is most unlikely from all that is otherwise known, that the tissues of our experimental animals are chemically imperfect or essentially unlike those of normally fed rats which presumably do contain glycocoll and lysine groups. Have we heretofore underrated the ultimate synthetic capacities of animal cells?[23]

The observation that animals long maintained on diets of the character used in our feeding trials voraciously eat the feces of normally fed rats led us to experiment in another direction. It has been noted as a result of this that in a not inconsiderable number of instances the feeding of small portions of "normal" rat feces tended to check the decline of rats kept on pastes of isolated food substances containing the earlier salt mixture. The possibility of altering the bacterial flora of the alimentary tract by dietetic conditions at once suggests itself in this connection, and reference may be made to the significant studies of Herter and Kendall,[24] among others, which elucidate this question. To what extent is the cooperation of bacteria either essential or useful in the alimentary functions? This is, indeed, still a debated question.[25] But one can not dispel the idea that bacteria might, after all, enter into reconstructive reactions which may furnish new nitrogenous complexes from amino-acids. Viewed in this light, the immediate hydrolysis products of our foodstuffs may become available only after they have in greater or less part been reconstructed by the preeminently synthetic symbiotic bacteria into products of more uniform character, possibly widely different from the original intake. Nucleoprotein synthesis, for example, may thus become referable to bacterial intervention; and the subtle influence of the indeterminable non-protein factors may lie in some measure in the regulation which they exert upon the micro-organisms of the gastro-intestinal tract.[26] In any event such suggestions need to be dealt with.

It is hoped to continue these nutrition studies, the possible scope of which has barely been indicated in what has gone before. They seem to us to justify the effort which has been involved. Indeed only by unremitting regard for details, such as the careful purification and preparation of the materials fed and attention to the animals, can the uncertain factors be limited, comparable results obtained and definite conclusions safely drawn. We realize that only a beginning has been made, and believe that further progress is possible.

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[23] One is reminded of the recent studies of Knoop, *Zeitschrift für physiologische Chemie*, 1910, LXVII., p. 489, and Embden and Schmitz, *Biochemische Zeitschrift*, 1910, XXIX, p. 423, bearing on such possibilities. Cf. Mendel, *Ergebnisse der Physiologie*, 1912, XI.

[24] Herter, "The Common Bacterial Infections of the Digestive Tract," The Macmillan Co.; Herter and Kendall, *Journal of Biological Chemistry*, 1910, VII., p. 203; Kendall, *Journal of the American Medical Association*, April 15, 1911.

[25] Nuttall and Thierfelder, *Zeitschrift für physiologische Chemie*, 1895, XXI., p. 109; Schottelius, *Archiv für Hygiene*, 1908, 67, pp. 177–208.

[26] Cf. Armsby, "The Nutritive Value of the Non-protein of Feeding Stuffs," Bureau of Animal Industry, Bulletin 139, 1911.